



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

Address: COMMISSIONER FOR PATENTS

P.O. Box 1450

Alexandria, Virginia 22313-1450

www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/776,643	02/12/2004	Helen Vivian Hsieh	82880	1755
46851 7590 08/19/2008 David W. Highet, VP & Chief IP Counsel Becton, Dickinson and Company (Morgan, Lewis & Bockius, LLP) 1 Becton Drive, MC 110 Franklin Lakes, NJ 07417-1880				
EXAMINER				
DESAL, ANAND U				
ART UNIT		PAPER NUMBER		
1656				
MAIL DATE		DELIVERY MODE		
08/19/2008		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/776,643

**Applicant(s)**

HSIEH ET AL.

**Examiner**

ANAND U. DESAI

**Art Unit**

1656

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 May 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 43-83 is/are pending in the application.
- 4a) Of the above claim(s) 43-56, 58-77 and 80-83 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 57, 78 and 79 is/are rejected.
- 7) ☒ Claim(s) 57 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 12 February 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date 20050218; 20050728
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date: \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Election/Restrictions***

1. Applicant's election with traverse of the species identified as a binding protein with at least two luminescent reporter group conjugated thereto in the reply filed on May 19, 2008 is acknowledged. Applicant's state that claims 78 and 79 read on the elected species. The traversal is on the ground(s) that the species are not necessarily mutually exclusive. A single embodiment of the present invention may comprise all three of the alleged mutually exclusive species. This is not found persuasive because the species recite mutually exclusive characteristics and the species are not obvious variants of each other based on the current record. The election of species will be withdrawn if applicants submit evidence or identify such evidence showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 43-56, 58-77, and 80-83 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on May 19, 2008.
3. Claims 57, 78, and 79 are currently under examination.

***Priority***

4. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 120. The priority date is January 4, 2002.

***Information Disclosure Statement***

5. The information disclosure statements (IDSs) submitted on February 18, 2005 and July 28, 2005 are being considered by the examiner. The reference lined through on the July 28, 2005 IDS were previously cited on the February 18, 2005 IDS form 1449.

***Oath/Declaration***

6. A new oath or declaration is required because inventor Terry Amiss has not dated the oath. The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

***Specification***

7. The disclosure is objected to because of the following informalities:
8. There is a hypertext link in the specification. Paragraph [0025] has a hypertext link. Suggest deleting the hypertext link.

9. The specification refers to mutated amino acid glucose/galactose binding proteins with particular amino acid modifications at particular locations without a recitation of the amino acid sequence with a SEQ ID NO: (see for example paragraph [0027]). Suggest identifying the protein with a SEQ ID NO: so as to convey to the public which mutated glucose/galactose binding proteins are being disclosed.

Appropriate correction is required.

#### ***Claim Objections***

10. Claim 57 is objected to because of the following informalities:
11. The claim recites modifications of an amino acid sequence at a particular residue location without reciting the reference for the amino acid position. Suggest placing a SEQ ID NO: for the mutated glucose/galactose binding protein to disclose to the public the mutated protein encompassed by the claim. It appears support is provided for the E. coli glucose/galactose binding protein identified on page 6 of the instant specification.
12. Appropriate correction is required.

#### ***Claim Rejections - 35 USC § 112, 1<sup>st</sup> paragraph, enablement rejection***

13. Claims 57, 78, and 79 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are rejected because of undue experimentation to practice the claimed inventions for the genus of mutated glucose/galactose peptides with the modifications recited. The undue experimentation arises due to the unpredictability based on the differing conditions of starting materials, such as the genus of mutated glucose/galactose binding proteins with luminescent labels that are implied to be able to detect variations in glucose and/or galactose concentration based on the structure of the composition. The claims as currently written are not limited to any particular mutated glucose/galactose binding protein, because no SEQ ID NOs are provided for the binding proteins. The claims encompass a genus of any mutated glucose/galactose binding protein.

In *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) eight factors should be addressed in determining enablement.

While the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection. The language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims. This can be done by making specific findings of fact, supported by the evidence, and then drawing conclusions based on these findings of fact. For example, doubt may arise about enablement because information is missing about one or more essential parts or relationships between parts which one skilled in the art could not develop without undue experimentation. In such a case, the examiner should specifically identify what information is

missing and why one skilled in the art could not supply the information without undue experimentation. See MPEP § 2164.06(a). References should be supplied if possible to support a prima facie case of lack of enablement, but are not always required. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). However, specific technical reasons are always required.

1) The nature of the invention: the instant claims are directed to a mutated glucose/galactose binding protein having modifications as recited in claim 57 and further comprising two luminescent reporter groups covalently coupled to said binding proteins. The two reporter groups can be either IANBD used twice, or IANBD along with Texas Red as claimed in claim 79.

3) The predictability or unpredictability of the art: & 6) The quantity of experimentation necessary: & 7.) The state of the prior art: the prior art has shown a large quantity of experimentation is often necessary to overcome the unpredictable nature of protein modifications. Marvin and Hellinga (IDS 2/18/2005; document page 3) disclose the unpredictability of using any fluorophore as a conjugate by disclosing that acrylodan and IANBD are sensitive to changes in the polarity of their microenvironment (see page 10, section titled Microenvironment of the Fluorophore Conjugates). Applicants own disclosure describes the state of the art, which discloses specific mutations of sites and/or attachment of certain reporter groups may act to modify a binding constant in an unpredictable way. Applicants also state that it is currently not possible to predict the effect on either the binding constant or the selectivity based on the position of any reporter group, or amino acid substitution in the protein (see paragraph [0009] of instant disclosure).

Consequently, there would be a large quantity of experimentation necessary to determine what conditions are required to disclose to the public a genus of mutated glucose/galactose binding proteins with two reporter luminescent groups that still retain the implied function of measuring the variation in glucose and/or galactose concentration that is correlated to the luminescent signal generated.

4) The amount of direction or guidance presented: & 5) The presence or absence of working examples: the specification discloses the modification of a single species of *E. coli* mutated glucose/galactose binding protein conjugated with two luminescent reporter groups to correlate varying glucose/galactose concentrations.

How would one of skilled in the art use the composition if it is unknown what other members of the genus of mutated peptides are capable of being modified and still retain a correlation of sensing a change in glucose and/or galactose concentration?

8.) Level of skill in the art: the level of skill in this art is high, at least that of a doctoral scientist with several years of experience in the art.

In consideration of the Wands factors, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching, and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

### ***Conclusion***

14. No claims are allowed.



Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANAND U. DESAI whose telephone number is (571)272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on (517) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

August 18, 2008

/ANAND U DESAI, Ph.D./  
Patent Examiner, Art Unit 1656